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10/563,744	06/02/2006	Josephus Carolus Maria Holthuis	03-702-A	5010

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EXAMINER	
CHOWDHURY, IQBAL HOSSAIN	

ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/563,744	HOLTHUIS ET AL.	
	Examiner	Art Unit	
	IQBAL H. CHOWDHURY	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-63* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-63 are currently pending in this application.

This application is a 371 of PCT/NL04/00488.

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group, I claim(s) 1-11 (in part), drawn to an isolated polypeptide comprising the motifs of (a), (b) or (c) having sphingomyelin synthase (SMS) activity.

Group, II claim(s) 1-11 (in part), drawn to an isolated polypeptide comprising the motifs of (a), (b) or (c) having ethanolamine phosphorylceramide synthase (EPCS) activity.

Group, III claim(s) 1-11 (in part), drawn to an isolated polypeptide comprising the motifs of (a), (b) or (c) having phosphotidylcholine:glycoprotein/glycolipid cholinephosphotransferase (PCGCPT) activity.

Group, IV claim(s) 12-20 (in part), 24, 30, drawn to an isolated polynucleotide encoding a polypeptide having SMS activity, a plasmid, vector, transformed host cell and process for producing said SMS polypeptide.

Group, V claim(s) 12-20 (in part), 24, 30, drawn to an isolated polynucleotide encoding a polypeptide having EPCS activity, a plasmid, vector, transformed host cell and process for producing said polypeptide.

Group, VI claim(s) 12-20 (in part), 24, 30, drawn to an isolated polynucleotide encoding a polypeptide having PCGCPT activity, a plasmid, vector, transformed host cell and process for producing said SMS polypeptide.

Group, VII claim(s) 21, drawn to a process for producing sphingomyelin by using a transformed microorganism expressing SMS enzyme.

Group, VIII claim(s) 25, drawn to a process for producing ethanolamine phosphorylceramide by using a transformed microorganism expressing EPCS enzyme.

Group, IX claim(s) 31, drawn to a process for producing phosphotidylcholine-substituted glycoprotein or phosphotidylcholine-substituted glycolipid by using a transformed microorganism expressing PCGCPT enzyme.

Group, X claim(s) 22-23, drawn to a method for identifying a compound which modulates SM synthesis by using a transformed microorganism expressing SMS.

Group, XI claim(s) 26-27, drawn to a method for identifying a compound which modulate EPC synthesis by using a transformed microorganism expressing EPCS enzyme.

Group, XII claims 28-29 (in part), drawn to a method for applying said compound for medical use, which modulates SMS activity.

Group, XIII claims 28-29 (in part), drawn to a method for applying said compound for medical use, which modulates EPCS activity.

Group, XIV claims 34-35, drawn to a method for applying said compound for medical use, which modulate PGCCPT activity.

Group, XV claim(s) 32-33, drawn to a method for identifying a compound which modulate PGC synthesis by using a transformed microorganism expressing PGCCPT enzyme.

Group, XVI claim(s) 36-37 (in part), drawn to a process for isolating a desired gene encoding an enzyme having SMS enzyme activity.

Group, XVII claim(s) 36-37 (in part), drawn to a process for isolating a desired gene encoding an enzyme having EPCS enzyme activity.

Group, XVIII claim(s) 36-37 (in part), drawn to a process for isolating a desired gene encoding an enzyme having PGCCPT enzyme activity.

Groups, XIX claim(s) 38-46, 56-58 (in part), drawn to a method for determining whether a compound is capable of modulating an enzymatic activity displayed by a cell, wherein said enzyme is SMS.

Groups, XX claim(s) 38-46, 56-58 (in part), drawn to a method for determining whether a compound is capable of modulating an enzymatic activity displayed by a cell, wherein said enzyme is EPCS.

Groups, XXI claim(s) 38-46, 56-58 (in part), drawn to a method for determining whether a compound is capable of modulating an enzymatic activity displayed by a cell, wherein said enzyme is PGCCPT.

Group, XXII claim(s) 47 and 49 (in part), drawn to a method of use of a nucleic acid sequence as probe for detecting an isolated polypeptide comprising the motifs of (a), (b) or (c) having SMS enzyme activity.

Group, XXIII claim(s) 47 and 49 (in part), drawn to a method of use of a nucleic acid sequence as probe for detecting an isolated polypeptide comprising the motifs of (a), (b) or (c) having EPCS enzyme activity.

Group, XXIV claim(s) 47 and 49 (in part), drawn to a method of use of a nucleic acid sequence as probe for detecting an isolated polypeptide comprising the motifs of (a), (b) or (c) having PGCCPT enzyme activity.

Groups, XXV claim(s) 48 and 49 (in part), drawn to a method of use of a nucleic acid sequence for detecting an isolated polypeptide as depicted in figure 8, such as human SMS1.

Groups, XXVI claim(s) 48 and 49 (in part), drawn to a method of use of a nucleic acid sequence for detecting an isolated polypeptide as depicted in figure 8, such as human SMS2.

Groups, XXVII claim(s) 48 and 49 (in part), drawn to a method of use of a nucleic acid sequence for detecting an isolated polypeptide as depicted in figure 8, such as human SMSr.

Groups, XXVIII claim(s) 48 and 49 (in part), drawn to a method of use of a nucleic acid sequence for detecting an isolated polypeptide as depicted in figure 8, such as C. elegans SMS1.

Groups, XXIX claim(s) 48 and 49 (in part), drawn to a method of use of a nucleic acid sequence for detecting an isolated polypeptide as depicted in figure 8, such as C. elegans SMS2.

Groups, XXX claim(s) 48 and 49 (in part), drawn to a method of use of a nucleic acid sequence for detecting an isolated polypeptide as depicted in figure 8, such as C. elegans SMS3.

Groups, XXXI claim(s) 48 and 49 (in part), drawn to a method of use of a nucleic acid sequence for detecting an isolated polypeptide as depicted in figure 8, such as C. elegans SMSr.

Groups, XXXII claim(s) 48 and 49 (in part), drawn to a method of use of a nucleic acid sequence for detecting an isolated polypeptide as depicted in figure 8, such as C. elegans SMSdr.

Groups, XXXIII claim(s) 48 and 49 (in part), drawn to a method of use of a nucleic acid sequence for detecting an isolated polypeptide as depicted in figure 8, such as P. falciparum SMS1.

Groups, XXXIV claim(s) 48 and 49 (in part), drawn to a method of use of a nucleic acid sequence for detecting an isolated polypeptide as depicted in figure 8, such as P. falciparum SMS2.

Groups, XXXV claim(s) 48 and 49 (in part), drawn to a method of use of a nucleic acid sequence for detecting an isolated polypeptide as depicted in figure 8, such as D. melanogaster SMSr.

Group, XXXVI claims 50-52, drawn to a method of screening an inhibitor of SMS as a cell death promoter.

Group, XXXVII claim(s) 53 (in part), drawn to a method of use of a nucleic acid sequence encoding an isolated polypeptide as depicted in figure 8, such as human SMS1for enhancing cell survival and/or cell growth.

Group, XXXVIII claim(s) 53 (in part), drawn to a method of use of a nucleic acid sequence encoding an isolated polypeptide as depicted in figure 8, such as human SMS2for enhancing cell survival and/or cell growth.

Group, XXXIX claim(s) 53 (in part), drawn to a method of use of a nucleic acid sequence encoding an isolated polypeptide as depicted in figure 8, such as human SMSr for enhancing cell survival and/or cell growth.

Group, XXXX claim(s) 53 (in part), drawn to a method of use of a nucleic acid sequence encoding an isolated polypeptide as depicted in figure 8, such as C. elegans SMS1for enhancing cell survival and/or cell growth.

Group, XXXXI claim(s) 53 (in part), drawn to a method of use of a nucleic acid sequence encoding an isolated polypeptide as depicted in figure 8, such as C. elegans SMS2 for enhancing cell survival and/or cell growth.

Group, XXXXII claim(s) 53 (in part), drawn to a method of use of a nucleic acid sequence encoding an isolated polypeptide as depicted in figure 8, such as C. elegans SMS3 for enhancing cell survival and/or cell growth.

Group, XXXXIII claim(s) 53 (in part), drawn to a method of use of a nucleic acid sequence encoding an isolated polypeptide as depicted in figure 8, such as C. elegans SMSr for enhancing cell survival and/or cell growth.

Group, XXXXIV claim(s) 53 (in part), drawn to a method of use of a nucleic acid sequence encoding an isolated polypeptide as depicted in figure 8, such as C. elegans SMSdr for enhancing cell survival and/or cell growth.

Group, XXXXV claim(s) 53 (in part), drawn to a method of use of a nucleic acid sequence encoding an isolated polypeptide as depicted in figure 8, such as P. falciparum SMS1 for enhancing cell survival and/or cell growth.

Group, XXXXVI claim(s) 53 (in part), drawn to a method of use of a nucleic acid sequence encoding an isolated polypeptide as depicted in figure 8, such as P. falciparum SMS2 for enhancing cell survival and/or cell growth.

Group, XXXXVII claim(s) 53 (in part), drawn to a method of use of a nucleic acid sequence encoding an isolated polypeptide as depicted in figure 8, such as D. melanogaster SMSr for enhancing cell survival and/or cell growth.

Groups, XXXXVIII claim(s) 54-55 (in part), drawn to a method for improving the yield of secretion of a polypeptide having SMS activity.

Groups, XXXXIX claim(s) 54-55 (in part), drawn to a method for improving the yield of secretion of a polypeptide having EPCS activity.

Groups, XXXXX claim(s) 54-55 (in part), drawn to a method for improving the yield of secretion of a polypeptide having PCGCPT activity.

Groups, XXXXXI claim(s) 59-63 (in part), drawn to a method for targeting of a first polypeptide having SMS activity to a different cellular compartment by fusing with signal sequence of second polypeptide.

Groups, XXXXXII claim(s) 59-63 (in part), drawn to a method for targeting of a first polypeptide having EPCS activity to a different cellular compartment by fusing with signal sequence of second polypeptide.

Groups, XXXXXIII claim(s) 59-63 (in part), drawn to a method for targeting of a first polypeptide having PCGCPT activity to a different cellular compartment by fusing with signal sequence of second polypeptide.

For each inventions I-XXXXXIII above, restriction to one of the following is also required under 35 U.S.C. 121 and 372. Therefore, election is required of one of inventions I-XXXXXIII **and** one of inventions (A) – (K).

(A). protein of SEQ ID NO: 12 or a nucleic acid encoding SEQ ID NO: 12.

(B). protein of SEQ ID NO: 13 or a nucleic acid encoding SEQ ID NO: 13.

(C). protein of SEQ ID NO: 14 or a nucleic acid encoding SEQ ID NO: 14.

(D). protein of SEQ ID NO: 15 or a nucleic acid encoding SEQ ID NO: 15.

(E). protein of SEQ ID NO: 16 or a nucleic acid encoding SEQ ID NO: 16.

(F). protein of SEQ ID NO: 17 or a nucleic acid encoding SEQ ID NO: 17.

(G). protein of SEQ ID NO: 18 or a nucleic acid encoding SEQ ID NO: 18.

(H). protein of SEQ ID NO: 19 or a nucleic acid encoding SEQ ID NO: 19.

(I). protein of SEQ ID NO: 20 or a nucleic acid encoding SEQ ID NO: 20.

(J). protein of SEQ ID NO: 21 or a nucleic acid encoding SEQ ID NO: 21.

(K). protein of SEQ ID NO: 22 or a nucleic acid encoding SEQ ID NO: 22.

2. The inventions listed as Groups I-XXXXXIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The polynucleotides encoding a polypeptide either SMS, EPCS or PCGCPT of Groups III-VI, polypeptide SMS, EPCS or PCGCPT of Groups I-III, each comprises unrelated and chemically distinct entities. The only shared technical feature of these groups is that they all relate to polynucleotides encoding polypeptides of SMS, EPCS or PCGCPT or polypeptides SMS, EPCS or PCGCPT. However, this shared technical feature is not a "special technical feature" as defined by PCT Rule 13.2 as it does not define a contribution over the art. The polypeptides SMS, EPCS or PCGCPT of are known in the art (Luberto et al. 1998, JBC, 273(23): 14550-14559, see IDS; Nagiec et al. 1997, JBC 272(15): 9809-9817; and Khan et al. 1990, JBC 265(2): 700-705). Thus, DNAs encoding SMS, EPCS or PCGCPT or polypeptides SMS, EPCS or PCGCPT and method of use thereof do not make contribution over the prior art.

3. The methods of Groups VII-IX do not share any "special technical feature" with Groups I-III as the polypeptides of Groups I-III are neither made nor used by the method of Groups VII-IX.

4. The methods of Groups X-XII do not share any "special technical feature" with Groups I-III as the polypeptides of Groups I-III are neither made nor used by the method of Groups X-XII.

5. The methods of Groups XIII-XV do not share any "special technical feature" with Groups I-VI as the polypeptides of Groups I-III or polynucleotides of Groups IV-VI are neither made nor used by the method of Groups XIII-XV.

6. The methods of Groups XXII-XXXXXIII do not share any "special technical feature" with Groups I-III as the polypeptides of Groups I-III are neither made nor used by the method of Groups XXII-XXXXXIII.

7. The methods of Groups XXXXXI-XXXXXIII do not have unity of invention with each other as each methods comprises unrelated steps, and use different products, and produce different effects.

8. The proteins of Group (A)-(K) are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different nucleotides encoding proteins of Group (A)-(K), which are polypeptides having SMS, EPCS or PCGCPT enzymes activity, do not have special technical feature among each other because they all represent structurally different polypeptides and polynucleotide encoding them. As mentioned above, polypeptides having SMS, EPCS or PCGCPT enzymes activity are known

in the art and does not make contribution over the prior art. Therefore, they all lack special technical feature.

37 CFR 1.475 does not provide for multiple products and/or methods within a single application. Therefore, inventions of Group I – XXXXXIII lack unity of invention.

Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

(a) the inventions have acquired a separate status in the art in view of their different classification;

(b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;

(c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);

(d) the prior art applicable to one invention would not likely be applicable to another invention;

(e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected invention**.

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention.

If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection

are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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